Int. J. Epidemiol. Advance Access published January 13, 2005

International Journal of Epidemiology
doi:10.1093/ije/dyh388

Diet quality and subsequent cancer incidence and mortality in a prospective cohort of women

Volker Mai,[1]* Ashima K Kant,[2] Andrew Flood,[3] James V Lacey Jr,[4] Catherine Schairer[4] and Arthur Schatzkin[4]

Accepted 27 October 2004

Background We have previously reported on the utility of the Recommended Foods Score (RFS), a measure of overall diet quality, in detecting associations between diet and mortality in a cohort of older women. Using additional follow-up, we have now extended our analysis to detailed studies of associations between RFS and the mortality and incidence from common cancers.

Methods The RFS, the sum of 23 recommended food items consumed at least weekly, was computed from a 62-item food frequency questionnaire completed at baseline by 42 254 women with a mean age of 61 years. Multivariate adjusted relative risk (RR) of cancer mortality and incidence of the cancers for which we were able to obtain data in relation to quartiles of RFS were examined using proportional hazards regression analyses after a median follow-up period of 9.5 years.

Results We observed that RFS was inversely associated with total mortality (RR = 0.8; $P < 0.001$) cancer mortality (RR = 0.74; $P < 0.001$) as well as mortality from cancers of the breast (RR = 0.75; $P < 0.06$), colon/rectum (RR = 0.49; $P < 0.01$) and lung (RR = 0.54; $P < 0.001$). The risk of incident lung cancer (RR = 0.62; $P < 0.001$) was reduced in women in the highest vs the lowest quartile of RFS; for incident cancers of the breast, colorectum, endometrium, ovaries, and bladder, there was no RFS association.

Conclusion A dietary pattern reflecting a higher RFS was associated with decreased overall mortality in women, specifically cancers of the lung, colon/rectum, and to a lesser extent breast. Incidence was only decreased for lung cancers. These observations are consistent with the hypothesis that a high RFS dietary pattern, or associated lifestyle factors, might affect cancer progression and survival.

Keywords Diet, cancer, dietary pattern, mortality, diet quality, women

Introduction

Although diet is thought to contribute strongly to several major cancers,[1] only few associations between individual dietary components and site-specific cancers have been established.[2,3] In recent years, assessment of dietary patterns has emerged as an alternative to single nutrients or specific food groups for the study of diet and health associations. Dietary pattern analyses have the advantage of examining diets in a comprehensive way that might better represent the biological interdependence of individual nutrients.[4] The results of studies of association of dietary patterns with cardiovascular disease, type II diabetes, and hypertension have been promising.[5–7]

The few studies of dietary patterns in relation to cancer, however, have produced inconsistent findings. In a Swedish mammography cohort, the Recommended Foods Score (RFS) used as a measure of diet quality in the present study, was adapted to the Swedish diet and was found to be associated with a significant reduction in total mortality as well as mortality from the main causes of death including cancer.[8] In the same study, a Not Recommended Foods Score was associated with an

[1] Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, MD 21201, USA. [2]Department of Family, Nutrition and Exercise Sciences, Queens College of City University of New York, Flushing, NY 11367, USA. [3]Division of Epidemiology, University of Minnesota, Minneapolis, MN 55454, USA. [4]Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, 20892, USA.

* Corresponding author. Volker Mai, Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, 10 South Pine St. MSTF 9-34, Baltimore, MD 21201-1192, USA. E-mail: vmai@epi.umaryland.edu

increased risk for death from cancer but not with overall mortality. An inverse association between a high dietary guideline index score and cancer incidence was reported from the Iowa Women's Health Study;[9] however, when body mass index (BMI) and exercise were removed from the dietary guideline index, only an association with lung cancer remained significant. In the Health Professionals Follow-up study, adherence to a healthy eating index (HEI),[10] based on the *Dietary Guidelines for Americans*, was weakly associated with incidence of major chronic disease, including cancer in men.[11] The HEI was not associated with disease in a cohort of female nurses.[12] When this index was modified by incorporating dietary variables that are known risk factors of chronic disease, the resulting alternative healthy eating index (AHEI) was associated with major chronic diseases but not with cancer incidence in both men and women.[13] In contrast, adherence to a Mediterranean diet was associated with reduced mortality from coronary heart disease (CHD) as well as cancer.[14]

In dietary patterns determined by factor analysis, the 'Western' pattern, characterized by higher intake of refined grains, red meat, and high fat, was weakly associated with incidence of colon but not rectal cancer in the Nurses' Health Study.[15] However, in a Swedish mammography cohort, the 'Western' pattern was unrelated with colorectal cancer (CRC) incidence, but there was a suggestion of a protective effect of a 'healthy' dietary pattern, a diet high in fruits and vegetables, fish and poultry, cereal and whole-grain breads, fruit juice, and low-fat dairy products, in a subset of women <50 years old.[16] Neither the 'healthy' nor the 'Western' pattern were associated with breast cancer incidence in the same cohort.[17]

We previously used current food-based dietary guidance to develop RFS and analysed it in relation to risks of total mortality, mortality from CHD, stroke and cancer (all cancers combined) in the Breast Cancer Detection Demonstration Project (BCDDP) follow-up cohort.[18] The objective of the present study was to extend our previous work by examining the RFS in relation to organ-specific cancer deaths and incidences for those cancers for which we had sufficient numbers (mortality from cancers of the breast, colon/rectum, and lung, and incidence of cancers of the breast, colon/rectum, lung, bladder, endometrium, and ovary).

Subjects and methods

Study population

The BCDDP was a breast cancer-screening programme conducted by the National Cancer Institute (NCI) and the American Cancer Society. The project enrolled 283 222 women and ran from 1973 through 1980 at 29 screening centres in 27 cities across the US. The BCDDP follow-up cohort was established in 1979 from a subset of women enrolled in the original BCDDP.[19] The follow-up study comprised all 4275 women from the BCDDP who had been diagnosed with primary breast cancer, all 25 114 women who had undergone a breast biopsy that indicated benign breast disease and all 9628 women who had been recommended for breast biopsy or breast surgery but who did not have the procedure. In addition, the follow-up cohort included 25 165 women who neither underwent nor were recommended for biopsy during the BCDDP; these women were matched with the breast cancer and benign breast disease subjects on age, time of study entry, ethnicity, screening centre, and length of participation.

The BCDDP follow-up study has proceeded in several phases beginning with baseline interviews between 1979 and 1981. Altogether, 61 434 of the invited women (96%) gave informed consent and completed the baseline questionnaire, which was updated annually for up to 6 years by telephone interviews. Participants completed additional mailed questionnaires during three separate follow-up periods: 1987–89, 1993–95 and 1995–98. We contacted non-responders with additional mailings; if they failed to return a mailed questionnaire, telephone interviews were attempted. Each follow-up questionnaire updated existing data, collected information about additional presumed risk factors, and provided self-reports of any newly diagnosed cancers.

Ethics

The study was approved by the IRB of the NCI.

Dietary assessment

The 62-item Block/NCI food frequency questionnaire (FFQ) was administered in 1987–89. This FFQ, which captures usual dietary intake over the previous year, has been described, validated for the foods that contributed to the RFS, and evaluated elsewhere.[20] Estimates of the daily nutrient intake were calculated by software specifically designed for this FFQ.[21] The RFS has been described previously.[18] The RFS reflects compliance with the current dietary guidance of increasing consumption of fruits, vegetables, whole grains, lean meats or meat alternatives, and low-fat dairy. The RFS includes 23 FFQ items: apples or pears; oranges; cantaloupes; orange or grapefruit juice; grapefruit; other fruit juices; dried beans; tomatoes; broccoli; spinach; mustard, turnip or collard greens; carrots or mixed vegetables with carrots; green salad; sweet potatoes, yams or other potatoes; baked or stewed chicken or turkey; baked or broiled fish; dark breads like whole wheat, rye, or pumpernickel; cornbread, tortillas and grits; high-fibre cereals, such as bran, granola or shredded wheat; cooked cereals; 2% milk and beverages with 2% milk; and 1% milk or skimmed milk. The RFS is calculated by summing each of these 23 items that was consumed at least once a week, for a maximum score of 23.

Analytical cohort

We excluded women who did not complete the 1987–89 questionnaire, which was considered the baseline for this study. Of the 51 694 women who returned the mailed FFQ, we excluded 9437 (18.3%) women who skipped more than 10 items on their FFQ or whose answers were unreliable based on previous validation studies.[22] The final analytical cohort for the mortality analyses consisted of 42 254 subjects. For the analyses of incident cancers, we additionally excluded all subjects who reported any previous cancer, except non-melanoma skin cancer ($n = 5114$), resulting in a final cohort of 37 135 subjects.

The follow-up period for each subject in the mortality analyses extended from the completion date of the 1987–89 questionnaire until the date of the earliest of the following events: death, completion of 1995–98 questionnaire, or end of study date (December 1998). In the cancer incidence analyses, the date of cancer diagnosis was also considered a study

endpoint. For subjects who did not complete questionnaires subsequent to the one in 1987–89 but who were successfully contacted, the end of study date was the date of last contact during 1995–98. For those who could not be contacted but were not known to be deceased, the end of study date was calculated as the date their last questionnaire was completed plus the average cohort follow-up time subsequent to that questionnaire. Follow-up was achieved at least once after the 1987–89 questionnaire for 90.8% of the subjects.

Case ascertainment

Deaths were identified by linkage with the National Death Index (NDI) (93%) and/or the mailed questionnaire. The cause of death was determined from the death certificate. Incident cancer cases were identified through self-reports from the 1993–95 and 1995–98 questionnaires, death certificates, and by matching with state cancer registries. Medical records were obtained to confirm information. For breast cancer, the most frequent cancer in our cohort, 90% of the case identifications included a self-report of the disease from one of the follow-up questionnaires, and for only <5% of the cases did identification depend exclusively on linkage with the NDI. Identification of other cancers relied more heavily on NDI linkage with the highest percentage of cases being for lung cancer (30%). We verified the cases with pathology reports whenever possible. All self-reports of breast cancer and 94% of the self-reports of CRC were confirmed by the pathology reports. Given this high conformation proportion for the most prevalent cancers, we decided to include in our analysis all self-reported cancers from subjects for which we were unable to obtain pathology data.

Statistical analysis

We used Cox proportional hazards model (proc PHREG in SAS version 6.12) with age as the underlying time metric (adjusted by left truncation, subjects contributed follow-up time from the age at which they entered the cohort) to calculate relative risks (RRs).

We evaluated possible confounders by adding known risk factors individually and simultaneously to the unadjusted model. Covariates evaluated in multivariate models included race; smoking status (detailed smoking history in all lung cancer analyses); alcohol intake; BMI; energy intake; history of cancer, heart disease or diabetes; postmenopausal hormone use status; physical activity and non-steroidal anti-inflammatory drug (NSAID) use. We retained all potential confounders that were previously established risk factors in the final multivariate model. Covariates for usual alcohol intake (g of alcohol/week), smoking history (ever/never, number of cigarettes/day, pack years), BMI (calculated as weight in kg/height in m^2), physical activity (active enough to sweat at least once a week), menopausal hormone use status (yes, no, unknown) and level of education (high school graduate or less/at least some college education) were ascertained from the 1987–89 questionnaire. History of NSAID use was assessed with the 1993–95 questionnaire and classified as yes/no with respect to ever having been a regular user, defined as taking at least one tablet weekly over a period of at least 1 year (excluding Tylenol). Smoking variables included duration of smoking, amount of cigarettes smoked per day, and time since quitting smoking (if applicable). Screening variables for mammograms and colonoscopies were created with information from the 1993–95 and the 1995–98 questionnaires, the total number of mammograms during the study period was determined by adding for each subject the mammograms performed during the follow-up time.

All models were energy adjusted by including a continuous term for daily energy intake. However, the results were not significantly affected by: (i) excluding the term for energy intake from the models, (ii) including a variable for quartiles of total energy intake, (iii) using the density, and (iv) the residual method of energy adjustment.

Results

Table 1 presents the distribution of factors generally associated with overall mortality and incident cancer by quartiles of RFS. The median follow-up was 9.5 years. Detailed characteristics of the cohort have been described previously.[19] In short, the cohort consisted of mainly white, well-educated subjects. Women in the lower quartiles of the RFS had a lower energy intake and were less physically active; they were more likely to report a history of smoking and a lower level of education. The history of menopausal hormone use and reproductive characteristics were similar in all quartiles.

The previously reported inverse associations between RFS and all cause mortality, mortality from cancer, and mortality from CHD[18] remained significant although they were slightly attenuated after including 1700 additional deaths in four additional years of follow-up (Table 2). The association between RFS and mortality from stroke remained but was not statistically significant. Stratification by smoking status (former/current vs never) did not reveal significant differences in the observed associations between RFS and all cause mortality and mortality from cancer.

In order to identify the cancer site(s) that contributed most significantly to the observed reduction in total cancer mortality, and thus to evaluate which cancers were most strongly associated with RFS, we examined the risk of mortality from: (1) breast cancer, (2) CRC, (3) lung cancer, which cause most female cancer deaths in the US and (4) 'all other cancers' (Table 3). The RFS had a strong inverse association with deaths from CRC (P for trend < 0.01) and lung cancers (P for trend < 0.001), even after adjustment for known risk factors including energy intake, smoking, and NSAID use. Mortalities from breast cancer (P for trend $= 0.06$) and 'all other cancers' (P for trend $= 0.11$) were, however, less strongly inversely associated with RFS. Adjustment for breast cancer screening in the subset of subjects for which information on the frequency of mammograms was available attenuated the observed reduction in breast cancer mortality.

Incident lung cancer was inversely related to RFS (Table 4). This association was observed in former and current smokers as well as in subjects who never smoked, although owing to the low number of cases (53) the association did not reach significance for the latter. The associations between RFS and incident cancers of the breast and the colorectum, however, were not significant. Excluding cases that occurred during the first 2 years of follow-up did not significantly change these results (data not shown). Associations between RFS and both breast and CRC incidence were essentially null after

Table 1 Distribution of baseline characteristics of mortality and cancer by RFS[a]

	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Number of subjects	8890	12 071	9087	12 206
RFS, mean (range)	6.4 (0–8)	10.0 (9–11)	12.5 (12–13)	16.0 (14–23)
Age in years, mean (SE),	60.4 (0.09)	60.8 (0.07)	61.3 (0.08)	61.8 (0.07)
Energy intake, mean kcal/day (SE)	1089 (5.4)	1218 (4.8)	1291 (5.7)	1433 (5.1)
BMI, mean kg/m^2 (SE)	25.3 (0.05)	25.0 (0.04)	25.1 (0.05)	24.9 (0.04)
Follow-up time, mean (years)	9.40	9.48	9.53	9.55
White race (%)	85.6	87.4	88.8	87.2
12+ year's education (%)	84	88.3	90.3	91.5
Current smoker (%)	19.7	13.1	9.8	8.2
Currently drink alcohol (%)	45.9	49.5	52.3	53.4
Physically active (% greater than or equal to once a week)	38.6	50.5	56.4	64.2
History of heart disease or diabetes (%)	12.4	13.3	12.9	13.0
History of cancer (%)	14.2	14.9	14.7	14.9
NSAID use (% ever)	35.2	38.4	39.6	40.3
Menopausal hormone user (%)	17.1	18.9	18.9	19.8
Mammograms (% yearly)	23.0	26.4	28.4	29.7
Colonoscopy/sigmoidoscopy (% ever)	23.8	26.2	27.9	30.4
Parity, mean	2.48	2.47	2.49	2.49
Age at menarche, mean (years)	13.3	13.1	13.1	13.2
Age of menopause, mean (years)	52.2	52.3	52.5	52.4

[a] RFS is calculated by summing each of the 23 'healthy' items that was consumed at least once a week, for a maximum score of 23 (see Materials and Methods section).

Table 2 RR estimates for all cause mortality, mortality from cancer, mortality from coronary heart disease and mortality of stroke by quartile of RFS

	RFS Median (range)				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Trend (*P* value)
Total mortality					
Unadjusted RR (95% CI)	1.00	0.81 (0.75–0.89)	0.69 (0.62–0.76)	0.66 (0.61–0.73)	<0.001
Multivariate-adjusted RR (95% CI)	1.00	0.87 (0.80–0.95)	0.78 (0.71–0.86)	0.80 (0.73–0.88)	<0.001
Number of cases (n = 3724)	941	1092	718	973	
Cancer					
Unadjusted RR (95% CI)	1.00	0.85 (0.74–0.98)	0.78 (0.67–0.91)	0.67 (0.58–0.77)	<0.001
Multivariate-adjusted RR (95% CI)	1.00	0.88 (0.76–1.01)	0.83 (0.71–0.97)	0.74 (0.63–0.86)	<0.001
Number of cases (n = 1473)	363	435	309	366	
CHD					
Unadjusted RR (95% CI)	1.00	0.72 (0.56–0.94)	0.63 (0.48–0.84)	0.58 (0.44–0.75)	<0.001
Multivariate-adjusted RR (95% CI)	1.00	0.79 (0.61–1.03)	0.76 (0.56–1.01)	0.75 (0.57–1.00)	0.05
Number of cases (n = 416)	113	118	81	104	
Stroke					
Unadjusted RR (95% CI)	1.00	0.87 (0.62–1.20)	0.57 (0.38–0.84)	0.60 (0.42–0.85)	0.01
Multivariate-adjusted RR (95% CI)	1.00	0.91 (0.66–1.28)	0.63 (0.42–0.95)	0.71 (0.49–1.03)	0.18
Number of cases (n = 246)	64	80	41	61	

Covariate adjusted models included: education level; race; smoking status; alcohol intake; BMI; energy intake; history of cancer, heart disease, or diabetes; postmenopausal hormone use status; active enough to sweat at least once a week. Total mortality and cancer models were adjusted for history of cancer, and CHD and stroke models were adjusted for both history of heart disease and diabetes.

Table 3 Relative risk (RR) estimates for mortality from various cancers by quartile of RFS

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Trend *P*-Value
Breast cancer[a] ($n = 376$)	1.00	0.81 (0.62–1.07)	0.73 (0.54–1.00)	0.75 (0.56–1.00)	0.06
Screening adjusted[b] ($n = 100$)		1.08 (0.60–1.95)	0.96 (0.50–1.84)	1.43 (0.81–2.53)	0.17
Lung cancer[c,d] ($n = 279$)	1.00	0.75 (0.56–1.02)	0.71 (0.50–1.00)	0.54 (0.38–0.76)	<0.001
Colorectal cancer[c] ($n = 120$)	1.00	0.77 (0.48–1.23)	0.70 (0.42–1.18)	0.49 (0.29–0.84)	<0.01
Other cancers[c] ($n = 698$)	1.00	1.08 (0.86–1.34)	1.05 (0.83–1.34)	0.85 (0.67–1.08)	0.11

[a] RR (95% CI) adjusted for energy intake, smoking (ever/never), NSAID use, BMI, age at menarche, age at menopause, parity, alcohol intake.

[b] RR (95% CI) in addition adjusted for number of mammograms in phases 3/4.

[c] RR (95% CI) adjusted for energy intake, smoking (ever/never), NSAID use, and BMI.

[d] RR (95% CI) in addition adjusted for smoking duration and cigarettes/day.

Table 4 Relative Risk (RR) estimates for incidence of various cancers by quartile of RFS

Cancer site	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Trend *P* Value
Breast[a] ($n = 1586$)	1.00	1.04 (0.90–1.20)	1.08 (0.92–1.26)	1.17 (1.01–1.36)	0.08
screening adjusted.[a, b] ($n = 1472$)	1.00	1.00 (0.85–1.16)	0.99 (0.84–1.16)	1.05 (0.90–1.23)	0.81
Colon/rectum[c] ($n = 372$)	1.00	1.07 (0.80–1.43)	0.97 (0.70–1.33)	0.94 (0.69–1.27)	0.56
screening adjusted.[c,d] ($n = 372$)	1.00	1.03 (0.77–1.37)	0.91 (0.66–1.25)	0.84 (0.62–1.14)	0.18
Lung[c,e] ($n = 353$)	1.00	0.81 (0.62–1.07)	0.69 (0.50–0.94)	0.62 (0.46–0.84)	<0.001
Endometrium[c] ($n = 263$)	1.00	0.78 (0.55–1.10)	0.91 (0.63–1.30)	0.87 (0.61–1.22)	0.33
Ovaries[c] ($n = 142$)	1.00	0.84 (0.54–1.33)	0.80 (0.48–1.30)	0.76 (0.47–1.22)	0.33
Bladder cancer[c] ($n = 78$)	1.00	1.25 (0.68–2.29)	0.59 (0.27–1.29)	1.02 (0.54–1.96)	0.62
All cancers[c] ($n = 2715$)	1.00	0.98 (0.88–1.09)	0.94 (0.84–1.06)	0.98 (0.88–1.09)	0.99

[a] RR (95% CI) adjusted for energy intake, smoking (ever/never), NSAID use, BMI, age at menarche, age at menopause, parity, and alcohol intake.

[b] RR (95% CI) in addition adjusted for number of mammograms in phases 3/4.

[c] RR (95% CI) adjusted for energy intake, smoking (ever/never), NSAID use, and BMI.

[d] RR (95% CI) in addition adjusted for colonoscopies (yes/no) in phases 3/4.

[e] RR (95% CI) in addition adjusted for smoking duration and cigarettes/day.

adjustments for cancer screening (mammograms and colonoscopies). For incident breast cancers, a positive association with RFS (RR = 1.34, 95% CI 1.08–1.67) was observed among subjects who had more than eight mammograms during follow-up. In a stratified analysis, we did not observe different associations between RFS and low- or high-grade breast cancers (data not shown). Postmenopausal hormone replacement therapy (HRT) was not a significant confounder or effect modifier in HRT-adjusted or stratified analyses in this study (data not shown). Incident cancers of the bladder, endometrium, and ovary were not significantly associated with the RFS, as can be seen in Table 4 (the numbers for mortality from these cancers were too low for a meaningful analysis).

Discussion

In this cohort, the RFS, an index of diet quality that captures aspects of dietary guidance regarding foods to be included in the diet and thus reflecting prevailing dietary guidance was inversely associated with overall mortality, CHD mortality, and overall cancer mortality. Moreover, the inverse association between the diet quality score and cancer mortality was significant for colorectal and lung cancers and was borderline

significant for breast cancers. Controlling for potential confounders that included established risk factors, e.g. detailed measures of smoking history, especially for all lung cancer analyses did alter the magnitude but not the direction of the observed associations. Excluding smokers (former and current) from the total mortality, cancer mortality, and lung cancer incidence analyses did not change the observed associations. Adjustment for the frequency of mammograms in the subset of subjects for which we had that information attenuated the reduction in mortality from breast cancer, indicating that screening might have confounded our unadjusted analysis.

Table 1 indicates that other lifestyle factors might have confounded our analysis and we cannot rule out the possibility that residual and unmeasured confounding may at least partially explain the observed associations. Furthermore, RFS may not be the causal factor for the observed associations but rather a marker for a healthy lifestyle in general.

We note that the dietary patterns used in this study were derived from a single FFQ. It is likely that dietary patterns of women in this cohort would have changed somewhat over the 10 years of follow-up; however, the BCDDP study protocol did not include a repeat assessment of dietary intake. Therefore, it is possible that these dietary changes have contributed to the attenuation of previously observed associations. We also acknowledge that measurement errors intrinsic to the use of a FFQ could have affected our findings. It is possible, with respect to the FFQ, that a multifactorial index like the RFS produces less misclassification than a single nutrient or food, but this is conjectural and awaits further methodological investigation.

Because mortality events reflect factors affecting both cancer incidence and survival, the question remains whether RFS is important in the aetiology of malignant disease or the prognosis in already diagnosed cancer. In an attempt to resolve this issue, we examined RFS in relation to cancer incidence in this cohort of older women. Except for lung cancer, the inverse association for RFS did not hold for the several cancer sites for which we had incidence data: breast, colorectum, endometrium, ovary, and bladder. This suggests that a dietary pattern reflecting a higher RFS is associated with those factors that prolong life in women already diagnosed with these cancers. We acknowledge that mortality is a more complex endpoint that is strongly influenced by factors such as treatment, screening practice, and severity of disease. Thus, it is possible that other unmeasured variables that are also associated with diet might have confounded our observations.

When we analysed the associations between RFS and incident breast cancer and CRC the inverse associations we had observed for fatal disease disappeared. We attempted to determine whether screening might have confounded this analysis by adjusting for the frequency of mammograms and colonoscopies in the breast cancer and CRC analyses. Adjustment for screening did indeed move the RR for incident breast cancer closer to the null and the RR for CRC towards an inverse association (Table 4), indicating that screening behaviour confounded our unadjusted analysis to some degree.

Mortality from cancer is affected to varying degrees by treatment as well as stage of cancer progression at time of detection. Thus, associations between diet quality and cancer death might be confounded by screening habits and treatment choice. The observation that mortality from CRC, for which screening and treatment have strong effects on the outcome, and mortality from lung cancer, for which screening and treatment have weaker effects on the outcome, show similar associations with RFS in this study argues somewhat against confounding by screening or treatment in the mortality analyses. Although in all lung cancer analyses we adjusted for smoking history to the best of our ability, some potential for confounding by this strong predictor of disease remains.

In a recent report, RFS and AHEI (a complex index derived from servings/day of vegetables, fruit, nuts/soy; ratio of white to red meat; g/day of cereal fibre, % energy from *trans* fatty acids; PUFA:SFA; duration of multivitamin use; and servings/day of alcohol) were compared for their relative ability to predict the risk of chronic diseases in two well-established large cohorts.[13] The authors concluded that AHEI was superior to RFS in detecting associations between diet quality and chronic disease. In that study RFS was based on weekly consumption of 49–56 items from an ~130-item FFQ. However, their modified RFS is not directly comparable with ours. It is weighted even more heavily towards fruit and vegetable intake (75%) than our score (65%). Their analysis did not detect any association between either one of the dietary scores and cancer (incidence + mortality combined), similar to our finding that total cancer incidence was not associated with RFS. However, we report here a strong association between RFS and cancer mortality and lung cancer incidence. Unfortunately, the dietary information obtained from the 62-item FFQ is limited and does not allow us to calculate a meaningful AHEI.

We cannot completely exclude the possibility that early malignant lesions might have affected the dietary intake or the report thereof by subjects who eventually died from cancer, which could distort our observations. Owing to the ~10 years of follow-up and the similar results of an earlier report from this cohort, this is unlikely to be an important factor in our study. Furthermore, the exclusion of incident cancers that occurred during the first 2 years of follow-up did not change our results.

Even after adjustment for potential confounders, including cancer screening, the associations between RFS and incident CRC and breast cancer were not significant, in contrast to the strong inverse association observed between RFS and CRC mortality and the more moderate association between RFS and breast cancer mortality. These data are consistent with the hypothesis that for breast and CRC a healthy diet might affect progression and survival, although we could not rule out the possibility that lifestyle factors, such as cancer screening, might contribute to the reductions in mortality. The potential of dietary interventions as an adjuvant to conventional treatment in improving cancer survival needs to be rigorously evaluated. Currently, studies that will evaluate the role of diet in survival after treatment for early breast cancer are in progress.[23] Complex dietary changes associated with a macrobiotic diet have been proposed to improve cancer survival,[24] but scientific data supporting such claims are largely missing. In the past, diet has mostly been studied as a means of cancer prevention; it might be timely to extend dietary studies to the period after cancer has been diagnosed. Future prospective studies of the associations between diet and cancer survival should be designed to achieve sufficient power to allow the investigation of potential confounding/effect modification by cancer stage, grade, and treatment.

Acknowledgements

The authors would like to thank the women who volunteered to participate in the BCDDP follow-up study. We would also like to thank Leslie Carroll at IMS, Inc., Silver Spring, MD, for computer support and Catherine Ann Grundmayer, Susan Engelhart, Lisa Kahle, and the BCDDP staff of Weststat, Inc., Rockville, MD, for assistance in collecting and processing data for the study. The authors wish to acknowledge the California Department of Health Services, Cancer Surveillance Section; the Florida Cancer Data System under contract to the state Department of Health; the Maryland Cancer Registry, Maryland Department of Health and Mental Hygiene; the Michigan Cancer Surveillance Program within the Division for Vital Records and Health Statistics, Michigan Department of Community Health; the Division of Health Statistics, Pennsylvania Department of Health; the Tennessee Cancer Registry; the Texas Department of Health; and the states of Arizona, Georgia, Hawaii, Idaho, Iowa, New Jersey, New York, North Carolina, Ohio, Oregon, and Rhode Island for providing data from their cancer registries for use in these analyses. The views expressed in this paper are solely those of the authors and do not necessarily reflect the opinions of any state agency listed above.

KEY MESSAGES

- A dietary pattern as measured by the RFS was associated with mortality in women.
- A high RFS was associated with lower cancer mortality.
- Incidence was only decreased for lung cancer.

References

[1] Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *J Natl Cancer Inst* 1981;**66:**1191.

[2] Potter JD. Nutrition and colorectal cancer. Cancer Causes and Control 1996;**7:**127–46.

[3] Willett WC. Diet and cancer. *Oncologist* 2000;**5:**393–404.

[4] Kant AK. Indexes of overall diet quality: a review. *J Am Diet Assoc* 1996;**96:**785–91.

[5] Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med* 2000;**343:**16–22.

[6] Hu FB, Manson JE, Stampfer MJ *et al*. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 2001;**345:**790–97.

[7] Appel LJ, Moore TJ, Obarzanek E *et al*. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997;**336:**1117–24.

[8] Michels KB, Wolk A. A prospective study of variety of healthy foods and mortality in women. *Int J Epidemiol* 2002;**31:**847–54.

[9] Harnack L, Nicodemus K, Jacobs DR, Jr, Folsom AR. An evaluation of the Dietary Guidelines for Americans in relation to cancer occurrence. *Am J Clin Nutr* 2002;**76:**889–96.

[10] Hann CS, Rock CL, King ID, Drewnowski A. Validation of the Healthy Eating Index with use of plasma biomarkers in a clinical sample of women. *Am J Clin Nutr* 2001;**74:**479

[11] McCullough ML, Feskanich D, Rimm EB *et al*. Adherence to the Dietary Guidelines for Americans and risk of major chronic disease in men. *Am J Clin Nutr* 2000;**72:**1223–31.

[12] McCullough ML, Feskanich D, Stampfer MJ *et al*. Adherence to the Dietary Guidelines for Americans and risk of major chronic disease in women. *Am J Clin Nutr* 2000;**72:**1214–22.

[13] McCullough ML, Feskanich D, Stampfer MJ *et al*. Diet quality and major chronic disease risk in men and women: moving toward improved dietary guidance. *Am J Clin Nutr* 2002;**76:**1261–71.

[14] Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean Diet and Survival in a Greek Population. *N Engl J Med* 2003;**348:**2599–608.

[15] Fung T, Hu FB, Fuchs C *et al*. Major dietary patterns and the risk of colorectal cancer in women. *Arch Intern Med* 2003;**163:**309–414.

[16] Terry P, Hu FB, Hansen H, Wolk A. Prospective study of major dietary patterns and colorectal cancer risk in women. *Am J Epidemiol* 2001;**154:**1143–49.

[17] Terry P, Suzuki R, Hu FB, Wolk A. A prospective study of major dietary patterns and the risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2001;**10:**1281–85.

[18] Kant AK, Schatzkin A, Graubard BI, Schairer C. A prospective study of diet quality and mortality in women. *JAMA* 2000;**283:**2109–15.

[19] Schairer C, Byrne C, Keyl PM, Brinton LA, Sturgeon SR, Hoover RN. Menopausal estrogen and estrogen-progestin replacement therapy and risk of breast cancer (United States). *Cancer Causes Control* 1994;**5:**491–500.

[20] Block G. A review of validations of dietary assessment methods. *Am J Epidemiol* 1982;**115:**492.

[21] National Cancer Institute. Information Management Services I, Block Dietary Data Systems. DIETSYS version 3.0 users guide. Bethesda, MD: National Cancer Institute. 1994.

[22] Block G, Hartman AM, Naughton D. A reduced dietary questionnaire: development and validation. *Epidemiology* 1990;**1:**58–64.

[23] Rock CL, Demark-Wahnefried W. Can lifestyle modification increase survival in women diagnosed with breast cancer? *J Nutr* 2002;**132:** 3504S–7S.

[24] Kushi LH, Cunningham JE, Hebert JR, Lerman RH, Bandera EV, Teas J. The macrobiotic diet in cancer. *J Nutr* 2001;**131:**3056S–64S.